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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/779,389	02/07/2001	Glenn McGall	18547-040820US	6566

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EXAMINER

FRIEND, TOMAS H F

ART UNIT	PAPER NUMBER
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1627

DATE MAILED: 06/28/2002 8

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Applicati n N .

09/779,389

Applicant(s)

MCGALL ET AL.

Examiner

Tomas Friend

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 28 March 2002.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-13 and 15-17 is/are pending in the application.
- 4a) Of the above claim(s) 16 and 17 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-13 and 15 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

Detailed Action

Change of Examiner's Name

The examiner's name has changed from Thomas Prasthofer to Tomas Friend.

Status of the Application

A response to an office action with amendment was received on 28 March 2002 (Paper No. 7).

Status of the Claims

Claims 1-17 were pending in the present application. Claims 16 and 17 were withdrawn from further consideration in Paper No. 5 as being drawn to a non-elected invention, the restriction having been traversed by applicants in Paper No. 4. Claim 14 has been cancelled as per applicants' request in Paper No. 7. Claims 1-13 and 15 are pending and examined on their merits.

Withdrawn Rejections

1. The rejections of claims 1-6, 8, and 10-15 under 35 U.S.C. 112, second paragraph, are withdrawn in response to applicants' amendment.
2. The rejection of claims 1, 2, 3, 8, 13, and 15 under 35 U.S.C. 102(b) as being anticipated by Terrett, N.K., "Combinatorial Chemistry" (1998) Oxford University Press, pp. 40-47, with Fodor et al. U.S. patent 5,424,186 (June 1995) cited to demonstrate the lack of degradation of oligonucleotides by ozone, is withdrawn in response to applicants' amendment.
3. The rejection of claims 1, 2, 3, 10, and 13 under 35 U.S.C. 102(b,e) as being anticipated by Fodor et al. U.S. patent 5,424,186 (June 1995) is withdrawn in response to applicants' amendment.

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4. The rejection of claims 1, 2, 3, and 7-15 under 35 U.S.C. 103(a) as being unpatentable over Terrett, N.K., "Combinatorial Chemistry" (1998) Oxford University Press, pp. 40-47 is withdrawn in response to applicants' amendment.

5. Claims 1, 2, 3, and 7-15 under 35 U.S.C. 103(a) as being unpatentable over Terrett, N.K., "Combinatorial Chemistry" (1998) Oxford University Press, pp. 40-47 and Fodor et al. U.S. patent 5,424,186 (June 1995) are withdrawn in response to applicants' amendment.

Maintained and New Rejections

The statutory basis for each of the following rejections may be found in a prior office action.

Maintained Rejections – 35 U.S.C. 112, second paragraph

6. The rejections of claims 7 and 9 under 35 U.S.C. 112, second paragraph, are maintained for reasons made of record in Paper No. 5.

Applicants argue that claims 7 and 9 are meant to encompass "*those methods in which a light source is used to irradiate the substrate from the backside (relative to the nascent nucleic acid formation, see Claim 7) and in which the light source may be from any position, but is focused and directed to the backside using, for example, mirrors (see Claim 9).*"

Applicants' argument has been carefully considered and found not to be persuasive. Claim 7 recites in part "*wherein said substrate is a planar support and is irradiated with light directed from a source at a position that is opposite the surface comprising said immobilized nucleotides.*" Claim 9 recites in part "*wherein said substrate is a planar support and is irradiated with light from a position opposite the surface comprising said immobilized nucleotides.*" The term "*opposite*" in claims 7 and 9 can be interpreted to mean "*on the other (opposite) side of the support*" but can also be interpreted to mean from the opposite side of a space between the light source and the immobilized nucleic acids (i.e. opposed to).

Maintained Rejections – 35 U.S.C. 103

7. Claims 4-6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Terrett, N.K., "Combinatorial Chemistry" (1998) Oxford University Press, pp. 40-47, Fodor et al. U.S. patent 5,424,186 (June 1995), and Urdea et al. U.S. Patent No. 4,517,338 (May 1985) for reasons made of record in Paper No. 5.

Applicants argue that the new limitation specifically reciting "*less than 5 ppb ozone*" overcomes the rejection because the cited references are silent with respect to ozone and the Urdea et al. reference includes method steps in an aqueous solvent.

Applicants' argument has been carefully considered and found not to be persuasive. Urdea et al., Column 8, lines 1-37, teaches that pressurized helium gas fills reagent reservoirs, reagent manifold, and reaction column. One of ordinary skill in the art would understand that helium gas at pressures positive pressures ranging from 5-25 psig fill all areas where reagents are stored and where reactions take place. Consequently, one of ordinary skill in the art would reasonably assume that the no ozone is present in the system during oligonucleotide synthesis and that the method inherently meets the presently claimed limitations with respect to ozone concentrations and degradation. One of ordinary skill in the art would have no reason to believe or suspect that pressurized helium contains 5 ppb or more of ozone.

8. Claims 4-6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Terrett, N.K., "Combinatorial Chemistry" (1998) Oxford University Press, pp. 40-47, Fodor et al. U.S. patent 5,424,186 (June 1995), and Brennan U.S. Patent No. 5,814,700 (September 1998) for reasons made of record in Paper No. 5.

Applicants argue that the new limitation specifically reciting "*less than 5 ppb ozone*" overcomes the rejection because the cited references are silent with respect to ozone.

Applicants' argument has been carefully considered and found not to be persuasive. Brennan, Column 8, lines 40-55, teaches that a common chamber containing reaction wells and nozzles is swept with inert gas to remove air and water traces from the chamber and that "*oxidation can be minimized, if not eliminated.*" Thus it would appear that the cited method inherently performs oligonucleotide synthesis at concentrations of ozone that are less than 5 ppb.

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One of ordinary skill in the art would not expect inert (presumably pure) inert gasses to contain 5 ppb or more ozone.

New Grounds of Rejection – 35 U.S.C. 103

9. Claims 1-3, 7-13, and 15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Terrett, N.K., “Combinatorial Chemistry” (1998) Oxford University Press, pp. 40-47, Fodor et al. U.S. patent 5,424,186 (June 1995), and Urdea et al. U.S. Patent No. 4,517,338 (May 1985).

The Terrett reference teaches various methods of synthesizing oligonucleotide arrays on a solid supports. On page 45 (just above figure 3.13), for example, it is disclosed that an octanucleotide array was produced in four hours. The method involves the activation of a support, attaching nucleotides to the support in defined regions that are not “*masked*,” the use of protecting groups, and cycles of nucleotide additions in which the pattern of the mask changes to allow reactions to occur at specified sites on the solid substrate (see page 43, second paragraph through page 45, first paragraph). The source of UV light used in light-directed parallel synthesis as disclosed on page 41 of Terrett is on the same side of the glass slide as the immobilized oligopeptide or oligonucleotide.

The Terrett reference does not explicitly teach an atmosphere of less than 5 ppb ozone, specified atmospheres for synthesis, a light source shining on the opposite side of a solid support from the array during VSLIPs synthesis, or packaging in an environment of less than 5 ppb ozone.

The Fodor et al. reference teaches a method for synthesizing oligonucleotides on a solid support using light-directed lithographic synthesis. Column 17, lines 8-12, teaches that either surface of a solid substrate (relative to the surface upon which synthesis is conducted) may be irradiated. Column 67, lines 12-17, teaches that a poly dT array was “*dried with N2 and stored in the dark under vacuum*” (i.e. less than 5 ppb ozone).

The Urdea et al. reference teaches a method for synthesizing polynucleotides (abstract). Urdea et al., Column 8, lines 1-37, teaches that pressurized helium is used to fill reagent reservoirs, a reagent manifold, and a reaction column. One of ordinary skill in the art would

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understand that helium gas at pressures positive pressures ranging from 5-25 psig fill all areas where reagents are stored and where reactions take place.

It would have been obvious to one of ordinary skill in the art at the time that the invention was made to conduct automated nucleic acid synthesis as per Fodor et al. and Terret in the presence of an inert gas such as helium or argon. One would have been motivated to do so to protect the reagents from reacting with water and oxidizing components in the atmosphere as taught by Urdea et al. One would have had reasonable expectation for success because the use of an inert gas environment during nucleic acid synthesis was well known at the time.

10. Claims 1-3, 7-13, and 15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Terrett, N.K., "Combinatorial Chemistry" (1998) Oxford University Press, pp. 40-47, Fodor et al. U.S. patent 5,424,186 (June 1995), and Brennan U.S. Patent No. 5,814,700 (September 1998).

The Terrett reference teaches various methods of synthesizing oligonucleotide arrays on a solid supports. On page 45 (just above figure 3.13), for example, it is disclosed that an octanucleotide array was produced in four hours. The method involves the activation of a support, attaching nucleotides to the support in defined regions that are not "*masked*," the use of protecting groups, and cycles of nucleotide additions in which the pattern of the mask changes to allow reactions to occur at specified sites on the solid substrate (see page 43, second paragraph through page 45, first paragraph). The source of UV light used in light-directed parallel synthesis as disclosed on page 41 of Terrett is on the same side of the glass slide as the immobilized oligopeptide or oligonucleotide.

The Terrett reference does not explicitly teach an atmosphere of less than 5 ppb ozone, specified atmospheres for synthesis, a light source shining on the opposite side of a solid support from the array during VSLIPs synthesis, or packaging in an environment of less than 5 ppb ozone.

The Fodor et al. reference teaches a method for synthesizing oligonucleotides on a solid support using light-directed lithographic synthesis. Column 17, lines 8-12, teaches that either surface of a solid substrate (relative to the surface upon which synthesis is conducted) may be irradiated. Column 67, lines 12-17, teaches that a poly dT array was "*dried with N2 and stored in the dark under vacuum*" (i.e. less than 5 ppb ozone).

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The Brennan reference column 8, lines 40-55 teaches that water and oxygen are to be excluded from reaction chambers in which phosphoramidites are used to synthesize nucleic acids because "*Phosphoramidites are sensitive to hydrolysis by tracing of water, and to oxidation by contact with air.*" The reference teaches that inert gas is used to "*sweep air and water traces from the chamber*" to reduce, if not eliminate hydrolysis and oxidation.

It would have been obvious to one of ordinary skill in the art at the time that the invention was made to conduct automated nucleic acid synthesis as per Fodor et al. and Terret in the presence of an inert gas. One would have been motivated to do so to protect the reagents from reacting with water and oxidizing components in the atmosphere as taught by Brennan. One would have had reasonable expectation for success because the use of an inert gas environment during nucleic acid synthesis was well known at the time.

11. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

12. This application contains claims 16 and 17 drawn to an invention nonelected with traverse in Paper No. 4. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

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13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Tomas Friend** at telephone number **(703) 308-4548**. The examiner can normally be reached on Monday, Tuesday, Friday, and Saturday 8:00-6:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jyothsna Venkat can be reached on (703) 308-2439. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-2742.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist at (703) 308-1235.



DR. JYOTHSNA VENKAT PH.D
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

Tomas Friend, Ph.D.
17 June 2002